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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,898	11/28/2001	Scott R. Presnell	00-108	1509

7590 12/23/2004

ZymoGenetics, Inc.
1201 Eastlake Avenue East
Seattle, WA 98102

EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,898	PRESNELL ET AL.	
	Examiner	Art Unit	
	Claire M Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *17-21,23 and 25-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,22 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-36* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-16, 22 and 24 remain rejected under 35 U.S.C. 1 12, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the previous Office action on pages 2-4.

Applicants argue that the specification presents multiple uses for the claimed polynucleotides, including detecting genetic variation in its sequence, *e.g.*, serving as a marker for the detection of an underlying disease, detecting translocations, aneuploidy, rearrangement and other chromosomal abnormalities involving the chromosomal region to which it maps. The argument has been fully considered, but is not persuasive. As stated in the previous Office action in the first paragraph of page 4:

> Even though the approximate chromosomal site of the DNA is provided (1p36. 11 region, p. 104-105), and there is a suggestion that aberration in this area of the chromosome are sometimes associated with cancerous cells or a predisposition to cancer, it is not disclosed which cancers are linked to that site. Also, because Zcytor19 DNA has not been shown to be involved in a cancer (though it could be a diagnostic marker for some cancers) and no aberration in Zyctor19 has been shown to be associated with a cancer, the mapping does not provide a specific utility. Also, the use as a chromosomal marker is not specific since there are many polynucleotides in the prior art that could be used to tag chromosome 1.

Once a change in gene copy number or sequence is detected and associated with a particular disease (for example, the expression of the 0.7kb nucleic acid probe of the 3'UTR of SEQ ID NO:1 sequence in certain cancerous tissues), then the gene may have a diagnostic use. However, in the instant case, except for the expression of the above probe in colon, endometrial and ovarian carcinoma, no genetic variation of the claimed polynucleotide has been linked with "an underlying disease". Without identification of the disease and the polynucleotide's link to that

disease (*i.e.*, how the nucleic acid or it's level is altered when the disease is present), the skilled artisan has only a invitation to experiment to determine an enabled use for the polynucleotide.

Applicants argue that the polynucleotide also has uses related to the encoded polypeptide, which a cytokine type II receptor and can be used for treating infections, detecting ligand-expressing tumors, and producing antibodies. The argument has been fully considered, but is not persuasive. As stated in the previous Office action on page 4:

> It is stated that the present encoded polypeptide, which has not actually been expressed, is member of the type II cytokine receptor family, possessing several features in common with type II cytokine receptors (p. 19, two paragraphs beginning line 12). Because it is not know what ligand Zcytor19 binds, what the physiological outcome of ligand binding would be or what diseases it is specifically associated with, the encoding nucleic acid does not have a specific utility.
> Even assuming the encode polypeptide of SEQ ID NO:1 is a type II cytokine receptor, one cannot use it for treating infections or detecting ligand-expressing tumors if one does not know what ligand it binds and the effect of particular ligand binding. While the polypeptide may be evolutionarily related to IL-10 receptors (p. 19, lines 24-26), without knowing what it does and what ligand activates it, one cannot use it without further undue experimentation. So while it may be possible to manipulate cytokine function to treat infection, for example, guidance must be provided about what cytokine(s) the receptor interacts with, what cell-types express it, and how its activation or inhibition will affect the disease. The specification of the instant application has not provided such guidance. Further, because the nucleic acid probe which was used diagnostically to detect certain carcinomas is from the untranslated region, one could not reasonably assume that the polypeptide encoded by any Zyctor19 form could be used diagnostically to detect cancer. Additionally, because SEQ ID NO:20 represents a soluble form, by definition a form that is not attached to a cell, the encoded soluble polypeptide will not be present in or on tumors (SEQ ID NO:21) so the soluble polypeptide would not have a diagnostic use as an expression product of a cancerous cell. As to the argument that the encoded polypeptide can be used to produce antibodies, if the artisan cannot use the polypeptide, an antibody which binds the polypeptide likewise is not enabled.

Applicants argue that the soluble receptor can be used to detect ligand-expressing solid tumors. The argument has been fully considered, but is not persuasive. If the ligand is not

known and, therefore, tumors expressing the ligand are not known, the soluble receptor cannot be used for diagnostic purposes without undue experimentation.

Applicants argue that not just the 0.7kb probe from the 3'UTR of SEQ ID NO:1 disclosed in Example 14 can be used to detect upregulation of a gene with diagnostic ability to distinguish between certain carcinomas and regular tissue, but "...that *any portion* of the cDNA as shown in SEQ ID NO:1, SEQ ID NO:18, or SEQ ID NO:20 can be used...." The argument has been fully considered, but is not persuasive. Three splice variants of Zcytor19 are disclosed (pages 19-21). It is unknown if other variants exist and which variant(s) comprises the 0.7 kb region of the 3'UTR of the probe expressed by colon, endometrial and ovarian carcinomas. Therefore, it is unknown to which splice forms the probe can hybridize (in *in situ* hybridization, for example) and which forms are expressed by which tumors. For example, ovarian carcinomas, while they have been shown to express a form that contains the 0.7kb 3'UTR of SEQ ID NO:1, may not express a truncated variant form. As stated in the previous Office action (p. 3, first paragraph), "Nor is it clear if other regions of SEQ ID NO: 1 would produce the same diagnostic results, for example, a 0.6kb fragment beginning at the ATG start site."

Claim Rejections - 35 USC § 102

Claims 1-5 remain rejected under 35 U.S.C. l02(b) as being anticipated by GenBank Accession Number M-358412.8 for the reasons of record set forth in the previous Office action on page 5.

Applicants argue that the instant application receives priority to provisionals 60/253,561 and 60/267,211 because those applications disclose uses of the currently claimed polynucleotide and, thus, meet the requirements of 35 USC 112, first paragraph. Neither provisional application discloses the enabled use as a probe using the 3' UTR of SEQ ID NO:1 for detection of colon, endometrial and ovarian carcinomas. Other asserted uses in the provisionals are not enabled (see discussion for the rejection under 35 USC 112, first paragraph, above relating to those uses).

Applicants argue that the GenBank sequence discloses only the *genomic* DNA with nothing to suggest the *cDNA* sequence. The claims are written in open language so that the claimed polynucleotide **comprises** the cDNA sequence or portion thereof. The genomic DNA

anticipates the claimed polynucleotides. The genomic DNA also encodes a polypeptide comprising the amino acid sequences listed in claims 1 and 3-5 (including splice variants).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 8:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (571) 273-8300. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

December 21, 2004

LORRAINE SPECTOR
PRIMARY EXAMINER